

EXHIBIT E

DECLARATION OF DR. KANWALJEET S. ANAND

I am Dr. Kanwaljeet S. Anand, M.B.B.S., D.Phil., FAAP, FCCM, FRCPCH who files this declaration under penalty of perjury. I am a pediatrician specialized in the care of critically ill newborns and children. I serve as a fully tenured Professor of Pediatrics, Anesthesiology, Perioperative & Pain Medicine at Stanford University School of Medicine, and as Director of the Pain/Stress Neurobiology Laboratory at Children's Hospital Research Institute. For more than 30 years, I have conducted intensive research and study on the development of pain/stress in human newborns, their development during early childhood, and long-term outcomes. I have authored 311 scientific publications (125 in the last 10 years), edited 9 books, and received numerous professional awards. My true and correct Curriculum Vitae is attached. I am personally familiar with Opioid Use Disorder in adult females and Neonatal Abstinence Syndrome and have reviewed the materials referenced below.

The President of the United States had declared a national medical emergency caused by the Opioid Crisis in America¹. The immediate effects of the Opioid Crisis, however, may be strikingly less consequential when compared to its effects on the individuals who were exposed to opioid drugs prenatally, many of whom were diagnosed with NAS. These children, through no fault of theirs, have been condemned to suffer from the short-term and long-term effects of opioid exposure from birth throughout their childhood, adolescence and into their adult lives. Though the current Opioid Crisis looms large on the thinking of social, medical, or government establishments, but its long-term impact is inestimable because of the pervasive and persistent effects of prenatal opioids on all aspects of an individual's development. Their cumulative burden of suffering, and the total impact of their exposures on all facets of our society is so huge and unparalleled in human history that this is truly the real emergency. Unless they are monitored/supported/treated NOW, the problems of these children will become intractable and unmanageable as they grow into adulthood, wiping away generations of human endeavor because of our short-sightedness. I offer the following statements for the Court's consideration:

Definitions

- Opioid Use Disorder (OUD) is defined in the DSM-5 as a problematic pattern of opioid use leading to clinically significant impairment or distress. OUD was previously classified as Opioid Abuse or Opioid Dependence in DSM-IV.
- OUD has also been referred to as "opioid addiction" in previous publications. Addiction is defined as a chronic, relapsing syndrome of psychological dependence and craving of a drug for its psychedelic, sedative, or euphoric effects; characterized by compulsion, loss of control, and continued use of a substance despite knowledge of its harmful effects².
- Infants and children are not "users" as defined under the DSM-5 criteria and are excluded from the class of persons suffering from OUD. Regardless, the birth mothers of children diagnosed with neonatal abstinence syndrome (NAS) would be included within the definition of OUD.
- Neonatal abstinence syndrome (NAS) or neonatal opioid withdrawal syndrome (NOWS) are terms used to denote a group of problems that occur in the children who were exposed to opioid or opiate drugs in the mother's womb. NAS is diagnosed clinically based on the clinical signs occurring in the 1 week after birth, characterized by neurologic hyperexcitability, gastrointestinal dysfunction, and autonomic instability. Most common neurologic signs include anxiety, agitation,

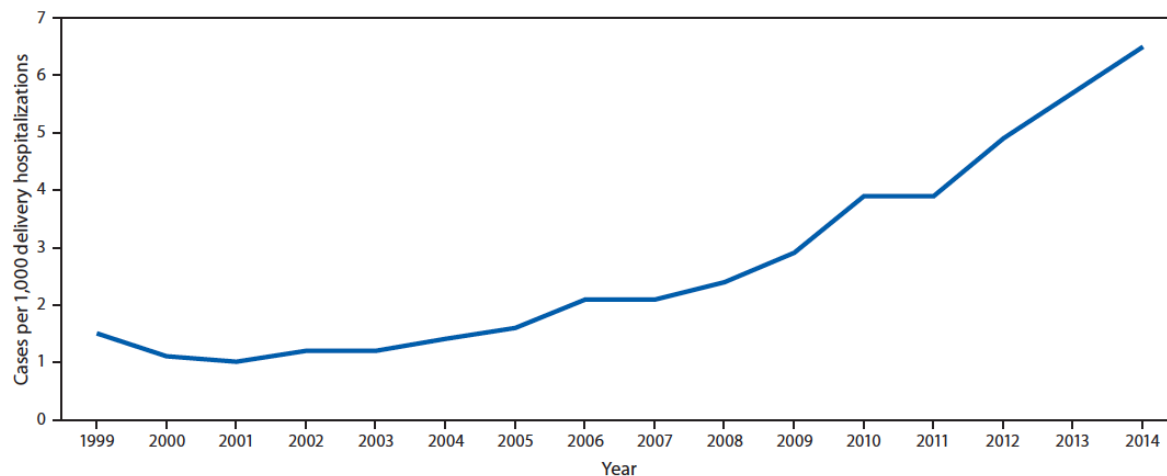
grimacing, insomnia, increased muscle tone/reflexes, exaggerated startle reflexes, high-pitched crying, tremors and abnormal movements, seizures; gastrointestinal symptoms include vomiting, diarrhea, poor sucking, dehydration; autonomic signs include elevated heart rate, respiratory rate, and blood pressure, fever, sweating, mottled skin, yawning, skin excoriation, cold extremities²⁻⁵.

- Notes: 1. Most clinicians diagnose NAS in children with modified Finnegan score of 8 or greater from two (2) consecutive assessments performed by a qualified healthcare practitioner with a minimum interval of 4 hours between the two consecutive NAS assessments⁶⁻⁹. Although the Finnegan NAS was criticized in various publications and alternatives were suggested, however, it is still the most widely used method for making a clinical diagnosis of NAS^{10,11}. Simplified versions of the Finnegan NAS scale were developed and cross-validated against the original Finnegan score but did not show any significant improvement in psychometric properties¹²⁻¹⁴. Other methods for making the NAS diagnosis include the Rivers opiate withdrawal tool¹⁵, the Lipsitz narcotic withdrawal score (cut-off score of 4 or more indicates NAS)¹⁴, the neonatal narcotic withdrawal index (cut-off score of 5 or more indicates NAS)¹⁶, and other less commonly used methods. Two recent studies have substantiated the validity of a clinical diagnosis for NAS coded within the patient's medical record at the time of hospital discharge^{17,18}. A quality improvement (QI) initiative showed increases in the accuracy and consistency of Finnegan NAS scoring by nurses, but the effects of this training were short-lasting¹⁹.
2. Although all children born to birth mothers suffering from OUD in pregnancy may or may not show signs/symptoms of NAS or NOWS, their brain development has been altered by repeated exposures to opioid drugs in the prenatal period. NAS signs/symptoms are the clinical manifestations resulting from sudden withdrawal of the prenatal opioid exposure, whereas the structural and functional alterations in their brain cells, connections, and architecture, as well as the brain damage from opioid-induced apoptosis (programmed cell death) occurs long before a child is born. These changes in brain development are permanent and will affect these children throughout their entire lifespan (see below). Therefore, we need to establish a class of individuals who were exposed to opioid drugs prenatally, particularly those who were diagnosed with NAS/NOWS after birth.
3. For the purposes of monitoring and surveillance, therefore, the following objective criteria will identify children with NAS and at risk for long-term neurodevelopmental consequences of prenatal opioid exposures:
- a) Diagnosis of NAS or NOWS documented in the child's medical record, for example, using the diagnostic codes of: P96.1/P04.49 (ICD-10 CM), 779.5/760.72 (ICD-9 CM)¹⁸; and/or
 - b) Monitoring of NAS/NOWS score(s) after birth, meeting the diagnostic criteria as defined above; and/or
 - c) Postnatal weaning of opioid drugs (morphine, methadone, buprenorphine, or other opioids); and/or
 - d) Children who are already listed in a national registry or other registries established for NAS²⁰; and/or
 - e) Toxicology screen of (a) maternal blood, urine, or hair analysis, (b) umbilical cord blood, (c) baby's meconium testing positive for opioids (excluding mothers who were prescribed opioids after the onset of, or for the purpose of treating labor pains, or for treating procedural pain).

The numbers of babies exposed to prenatal opioids annually

- 1) Based on trend analyses for birth mothers suffering from OUD in pregnancy, approximately 36,000 babies are likely to be born with prenatal opioid exposures in 2018²¹ (projected using the CDC birth rate data)²²⁻²⁴. CDC data show that the documented rate for birth mother OUD was 6.5 per 1,000 delivery hospitalizations in 2014 (MMWR, August 2018²¹). This is a conservative estimate, since it does not include babies delivered at home, at maternity clinics, or birthing centers. Epidemiological studies show that rates of birth mother OUD may be higher among women who use non-hospital birthing centers or prefer delivering their baby at home^{21,25-27}.
- 2) Using data from 1999 to 2014²¹, the National Average Annual increase in opioid exposed birth rates for mothers suffering from OUD was 0.39 per 1,000 delivery hospitalizations per year. This estimate averages the increases in birth mother OUD rates over 16 years of collected data, although the rate of increase was much greater in the last 5 years of data collection (Figure 1).

FIGURE 1. National prevalence of opioid use disorder per 1,000 delivery hospitalizations* — National Inpatient Sample (NIS),[†] Healthcare Cost and Utilization Project (HCUP), United States, 1999–2014



Even using this conservative yearly rate increase (3.9%) will give us prenatal opioid exposure rates increasing up to 8.45 per 1,000 delivery hospitalizations in 2019. However, if we project the prenatal opioid exposure rate increases from the past 5 years, National Average increases show an increased rate of 7.2% or 0.72 per 1,000 delivery hospitalizations per year. This will give us prenatal opioid exposure rates increasing to 10.1 per 1,000 delivery hospitalizations in 2019. These data are listed in **Table 1** on the next page. Table 1 also includes the “corrected” prenatal opioid exposure rates after adjusting for: (1) women undergoing detox before the baby’s birth, whose babies may not show signs of NAS; and (2) those women who do not deliver in a hospital (previous studies have reported higher OUD rates among these women).

Annual growth rate of individuals at risk for NAS

- 3) More than half (60-75%) of the individuals born to birth mothers with OUD in pregnancy are expected to be diagnosed with NAS as defined above^{21,28-36}. Those diagnosed with NAS are more likely than non-NAS individuals to have more significant exposures to prenatal opioids and to have developed subcellular and other physiological changes as a result of such exposures. CDC states that individuals at risk for NAS are “**clearly underestimated and under-reported**” but

the data available from 36 states in 2015 showed approximate increases of 7.2% occurring in each year between 2011 and 2015^{21,26,27,37,38}.

Table 1: Numbers of Individuals at risk for NAS: Trend analyses from 2014 to 2019

	National Average Increase 0.39/year (1999-2014 data)			National Average Increase 0.72/year (2011-2014 data)			Estimates including babies who detox <i>in utero</i> and those born in non-hospital settings		
	OUD rate/1000 hospital deliveries	Number of live- births: CDC data	Newborn s with prenatal opioid exposures	OUD rate/1000 hospital deliveries	Number of live- births: CDC data	Newborns with prenatal opioid exposures	Corrected OUD rates/1000 live births	Number of live- births: CDC data	Newborns with prenatal opioid exposures
2014	6.5	3,988,076	25,922	6.5	3,988,076	25,922	7.5	3,988,076	29,911
2015	6.89	3,978,497	27,412	7.22	3,978,497	28,725	8.5	3,978,497	33,817
2016	7.28	3,945,875	28,726	7.94	3,945,875	31,330	9.4	3,945,875	37,091
2017	7.67	3,853,472	29,556	8.66	3,853,472	33,371	10.3	3,853,472	39,691
2018*	8.06	3,776,403	30,438	9.38	3,776,403	35,423	11.1	3,776,403	41,918
2019*	8.45	3,738,639	31,591	10.1	3,738,639	37,760	11.9	3,738,639	44,490

*2018 Number of Live-births estimated with a 2% decrease in births from 2017; *2019 Number of Live-births estimated with a 1% decrease in births from 2018

Constellation of clinical conditions associated with NAS

- 4) Opioids are proven hazardous substances for prenatal human development. Thus, NAS is associated with premature birth, low birth weight, intrauterine growth retardation (IUGR), perinatal or neonatal mortality, increased birth defects, delayed cognitive development, long-term behavioral problems, ADHD, auditory deficits, speech delay, swallowing difficulty, gastro-esophageal reflux disease (GERD), digestive or gastrointestinal motility disorders, delayed feeding, failure to thrive, congenital neurological defects, and congenital heart defects³⁹⁻⁴⁵.

Time periods of interventions to achieve the best outcomes

- 5) For most of the conditions listed above, the best possible outcomes can only be achieved with proper management of NAS before hospital discharge, coupled with increased monitoring and surveillance, as well as active multi-disciplinary interventions that are initiated just after birth and continued for the child's entire childhood and adolescence (up to 18 years of age)^{30,39,46-56}.

Evidence suggesting that prenatal opioid exposure damages DNA

- 6) Huge amounts of published data substantiate the findings that prenatal opioid exposures alter genetic regulation and DNA structure, although many of these studies were performed in animal models⁵⁷. Almost 40 years ago, however, leading researchers discovered that prenatal opioid

exposure damages human DNA and/or prevents DNA repair occurring from other causes of DNA damage (e.g. UV light)⁵⁸. Since then, accumulating data have shown the progressive and persistent effects of repetitive prenatal opioid exposure on DNA fragmentation occurring in the developing human brain and in peripheral blood cells⁵⁸⁻⁷¹. More recently, several studies also documented the epigenetic effects of opioid addiction, capable of intergenerational and transgenerational transmission to the offspring of opioid addicts⁷²⁻⁸⁰. Although pregnant women were excluded from some of these studies, the underlying mechanisms are the same and will have extensive effects on the massive amounts of DNA synthesis occurring during prenatal human development^{66,81}.

Consequent to the opioid effects on human DNA cited above, a large number of studies have found a higher incidence of birth defects in the babies exposed to maternal opioids *in utero*⁴⁵. Seventeen (17) studies found opioid exposure linked with facial/oral defects (e.g., cleft lip, cleft palate, or others), heart defects (e.g., ventricular septal defects, atrial septal defects, hypoplastic left heart syndrome, pulmonary valve stenosis, conoventricular septal defects), limb deformities (e.g., clubfoot), visceral organ defects (e.g., gastroschisis), or neural tube defects (e.g., spina bifida)^{40,41,43-45}. Most of these conditions require multiple surgical operations and long-term medical care to support the optimal development of these severely affected children^{43,82}.

Long-term cognitive and behavioral outcomes of individuals diagnosed with NAS

- 7) Brain Development: Opioids have drastic and sustained effects on brain development in the fetal and postnatal periods, affecting the brain's size, architecture, networks and connections between brain cells, neurochemical and other functions of each cell, as well as the brain DNA's structure, its expression and regulation. Thus, prenatal opioid exposures have robust and long-term effects on the cognitive and behavioral outcomes of the individuals diagnosed with NAS⁸². Opioids affect brain development by disrupting oligodendrocyte development, altering the temporal sequencing and quality of nerve fiber myelination⁸³, decreasing the growth of nerve cell dendrites^{84,85} and their branching pattern complexity of pyramidal neurons in the cerebral cortex⁴⁰, and by suppressing cell proliferation and neuronal migration to the cortical plate⁸⁶. These effects may reduce regional brain volumes in the basal ganglia⁸⁷ and other brain areas⁸⁷⁻⁹⁰, with lower developmental potential.
- 8) Brain Growth: A large number of studies have reported lower birth weights and smaller head circumferences in opioid-exposed babies with relatively increased risks in those exposed^{20,36,87,91-99}. A controlled comparison showed that reduced fetal head and body growth in infants of opioid-dependent mothers were not explained by gestational age, cigarette smoking, area deprivation, infant gender, maternal age or parity¹⁰⁰. Given the limited maternal/environmental effects on head circumference, it is likely that the robust effects of opioid exposure on head circumference occur by reducing brain growth^{82,101}. This was confirmed in a pilot study of 16 infants, where volumetric MRI scans showed smaller whole brain volumes and basal ganglia volumes compared to age-matched population means⁸⁷. In another follow-up MRI study that included 38 youths in the opioid-exposed group and 44 youths in the non-exposed group (aged 17 to 22 years), the drug-exposed group displayed smaller brain volumes, smaller surface areas of the cerebral cortex, and thinner cortical mantles than unexposed youth⁸⁸.
- 9) Functional Effects: The consequences of this impaired brain growth are also pervasive, with altered dyadic interactions between mothers and infants¹⁰², impaired early development in all domains of the Griffith's Mental Development Scales¹⁰³, impaired visual acuity and visuomotor

functions (eye-hand coordination)^{101,103,104}, impaired language-related cognitive skills and executive functions^{105,106}, with inattention, hyperactivity, impulsivity, aggression, ADHD, other social and behavioral problems persisting into adolescence and even adulthood in those born to opioid-dependent mothers during pregnancy^{88,91,107-109}. Baldacchino et al. identified 200 follow-up studies of opioid exposures during pregnancy, but only 8 studies met inclusion criteria with 4 studies in infancy, 3 assessing preschool children, and 1 on school children^{110,111}. All these were case-control studies conducted within urbanized, low socioeconomic communities, with mothers exposed to either heroin or methadone. Five studies had data usable for meta-analysis, with a total of 218 opioid-exposed and 205 non-exposed children. In all outcomes opioid-exposed children had lower scores as compared to controls¹¹⁰.

- 10) Neurodevelopmental Consequences: Differences in neurodevelopment between children with and without exposure to prenatal opioids are related to the age at which they were assessed, with milder differences occurring at birth, greater differences during infancy and early childhood but widening gaps noted during school age and adolescence. Individuals with NAS at birth had impaired behavioral regulation, greater excitability and arousal, and poorer quality of their movements¹¹²⁻¹²¹. Among infants and toddlers, NAS was associated with impaired mental and language development as well as poorer neuromotor and psychomotor development before 24 months of age¹²². Because of the very limited roles for cognitive or executive functions in early childhood, studies performed in the younger age groups showed minimal differences in cognitive or executive functions with and without NAS^{123,124} (e.g., every infant is likely to fail an algebra test). In contrast, the Bayley Scales of Infant Development revealed more prominent neurodevelopment deficits, with greater vulnerability among boys than in girls¹²⁵⁻¹²⁷. Assessment in later childhood revealed differences in IQ, motor performance¹²⁸⁻¹³¹, language performance¹³², lower IQ scores, behavior and attention problems compared with unexposed children at 8.5 years of age^{107,108}. Children exposed to methadone prenatally also had elevated levels of aggression, fear, and anxiety^{91,130,133}. Even after controlling for their sociodemographic factors and birth mother's medical history, elevated symptoms of ADHD occurred in children who were exposed to prenatal opioids compared with children not exposed to opioids *in utero*^{91,130,134}.

A recent systematic review and meta-analysis of cohort studies of 1,455 children from birth to 18 years found that prenatal opioid exposures negatively impacted neurocognitive outcomes and physical/motor development from age 6 months onwards, and this association persisted until adolescence¹³⁵. The study could not differentiate between the contributions of prenatal opioid exposure vs. opioid treatment for NAS after birth and recommended that all NAS children should receive long-term monitoring, with social, emotional and educational support or intervention¹³⁵. The long-term effects of prenatal opioids on cognition tended to increase over time, even in those children who were adopted or placed in foster care, thus being exposed to minimal postnatal risk factors¹⁰⁷. NAS children discharged home with their birth mother, despite a longer hospital stay, had a higher likelihood of being referred for early intervention services (81%) compared to those placed in foster care (66%)¹³⁶.

- 11) Executive Functions: Executive functions are thinking skills that help us with the information processing, reasoning, planning, problem-solving, for coping with stress, regulating our emotions and managing our lives. As a child progresses through school, the executive functions assume greater importance in their academic success, goal setting, and employability¹³⁷. Children exposed to prenatal opioids have difficulties with information processing¹³⁸, poorer performance on a

vigilance task¹³⁹, lower overall executive functioning¹⁰⁵, significantly lower visual acuity¹⁰¹, impaired visual-motor and perceptual performances, and fewer goal-directed eye movements¹⁴⁰⁻¹⁴². Children with NAS were far more likely to have developmental delays and lower IQ¹⁴³, 2.3 times more likely to be hospitalized for neuropsychiatric disorders¹⁴⁴, 4.5 times more likely to be hospitalized for child abuse¹⁴⁴ and die during hospitalization¹⁴⁴, perform poorly on educational testing¹⁴⁵, and show cognitive disabilities requiring extra classroom therapies and services¹⁴⁶. CDC compared 1815 children with NAS and 5441 children without NAS (age 3-8 years). Children with NAS were more likely referred for disability evaluation (19.3% vs. 13.7%), have a learning disability (15.6% vs. 11.7%) and require classroom therapies (15.3% vs. 11.4%). These differences remained significant even after controlling for maternal smoking, maternal education, birth weight, gestational age, and/or NICU admission¹⁴⁶. Children with NAS had lower scores on standardized testing in grade 3; by grade 7, children with NAS were scoring lower than other children in grade 5 and showing progressively greater deficits¹⁴⁵. The increasingly complex cognitive processing and executive functioning required within a competitive high school environment place these children with NAS at progressively greater disadvantage and much higher likelihood of adverse outcomes, thus widening the gap between those with and without NAS.

- 12) **Neuropsychiatric outcomes:** Although Uebel et al. (2015) had found that more children with NAS were hospitalized with neuropsychiatric disorders (adjustment, conduct, anxiety, emotional, or speech disorders), three recent studies have highlighted the very high prevalence and distribution of mental health conditions among individuals with prenatal opioids. Using a Medicaid database, Sherman et al. (2019) found that half of all children with NAS were diagnosed with mental disorder before age 5, compared with 30% of all other births. Children with NAS were more likely to have conduct disturbances (2.7-fold), hyperkinetic syndromes (2.6-fold), adjustment difficulties (2.5-fold), stress/anxiety disorders (1.5-fold), emotional problems (1.9-fold), childhood-onset psychoses (1.7-fold), intellectual disabilities (2.3-fold), specific developmental delays (1.7-fold)¹⁴⁷. Mental health conditions were 1.6-fold more prevalent in children with a history of NAS than the opioid-exposed children without a history of NAS, and 1.4-fold higher among children with Medicaid vs. commercial health insurance (Table 2 from Conner et al., 2019)¹⁴⁸. From a longitudinally followed youth cohort (17-22 years) with prenatal opioid exposures (\pm other drugs) who were adopted/fostered before 1 year of age, Nygaard et al. (2019) found **2- to 8-fold higher lifetime risk of mental disorders** compared to matched controls¹⁴⁹. These risks mainly included

Diagnosis (ICD-9 code)	Commercial insurance (N=1,405,712)				Medicaid ^a (N=270,772)			
	NAS (N=190)		No NAS (N=1,405,522)		NAS (N=1,046)		No NAS (N=269,726)	
	N	%	N	%	N	%	N	%
Any mental health condition/diagnosis	68	35.8	313,021	22.3	511	48.9	81,814	30.3
Specific delays in development (315)	48	25.3	115,785	8.2	327	31.3	49,591	18.4
Disturbance of conduct (312)	11	5.8	37,120	2.6	113	10.8	10,879	4.0
Hyperkinetic syndrome of childhood (314)	13	6.8	102,770	7.3	94	9.0	9,372	3.5
Adjustment reaction (309)	9	4.7	63,295	4.5	75	7.2	7,799	2.9
Acute reaction to stress (308)	2	1.1	6,995	.5	49	4.7	8,123	3.0
Neurotic disorders (300)	9	4.7	60,749	4.3	43	4.1	7,365	2.7
Special symptoms or syndromes (307)	11	5.8	58,585	4.2	41	3.9	9,672	3.6
Disturbance of emotion specific to childhood and adolescence (313)	2	1.1	23,686	1.7	39	3.7	5,350	2.0
Intellectual disabilities (317-319)	1	.5	2,596	.2	37	3.5	4,074	1.5
Psychoses with origin specific to childhood (299)	8	4.2	26,860	1.9	32	3.1	4,752	1.8

^a Source: Sherman et al., 2019 (2). Adapted by permission from American Psychiatric Association Publishing.

major depression, alcohol abuse, ADHD, and aggressive behaviors even after controlling for age, gender, and caregivers' education. These children not only engaged in sex at younger ages and had **more sexual partners** compared to controls, but also experienced **suicidality** (28.8%), **psychoses** (17.7%), or **antisocial personality disorder** (15.6%) more often than their peers¹⁴⁹.

Such bleak outcomes portend a future tsunami of neurocognitive and neuropsychiatric disorders among the children and youth with NAS. The Opioid Crisis has increased over the past 20 years; therefore, multiple generations of such children and youth have been affected. While we continue to argue about priorities and preferences, these children are growing up – and every day that passes without the medical monitoring or supportive services being offered to these children, it makes their problems more and more intractable, imposing on them poorer outcomes and greater societal disadvantages.

Urgent need for more scientific investigations of individuals with NAS

Despite the recent flurry of scientific publications on this topic, there are numerous unanswered questions about the epidemiology, risk factors, diagnoses, management, and responses to therapy in the children with NAS. Therefore, there is an urgent need for a court-appointed Science Panel with the imperative to document the long-term outcomes of children exposed to prenatal opioids, through multiple, well-designed, large studies that prospectively enroll adult women with OUD and ensure good retention rates, to longitudinally follow their children with NAS at least until 18 years of age. All these children will require detailed neurocognitive and neuropsychiatric testing, as well as functional monitoring. Such tests are not available during routine doctor visits or other healthcare settings. To be explicit, these needs exist well-above and beyond the routine pediatric care and/or schooling required for non-opioid exposed children. These needs are not currently covered by Medicaid, or any private health insurance or any kind of Special-Ed funding. To obtain such data and to ensure that appropriate therapies and social services are offered, these children require detailed medical monitoring and surveillance through a well-coordinated, standardized, multidisciplinary, and nationally implemented protocol as described below. The results of such monitoring and surveillance must be regularly evaluated by the court-appointed Science Panel, so that accumulating data and scientific insights can be applied to the ongoing care of these children. To inform members of the Science Panel, they must be given access to all scientific and medical studies, data, experiments, white papers, research forms, or other materials related to the synthetic opioids, regardless of whether such materials had ever been provided to the FDA or whether they were protected assert trade secret protection.

Protocol for monitoring/surveillance of children diagnosed with NAS

- 1) Biological variability is based on genetic and epigenetic mechanisms, or factors related to the prenatal opioid exposure that manifested NAS (specific drugs, dosage, period(s) of pregnancy affected, detox or treatment effects, exposures to smoking, alcohol, or other drugs), as well as the postnatal treatments for NAS. All these will influence the child's long-term neurodevelopmental consequences resulting from NAS. Individual differences occurring between humans are difficult to determine specifically, but a common medical monitoring program is absolutely essential for all NAS victims because they are all at high-risk for common detrimental outcomes, associated with 'hidden' or latent conditions and disorders that can be ameliorated through medical monitoring, scheduled assessments, surveillance procedures and appropriate therapies. The proposed monitoring is different from that normally recommended in the absence of opioid exposures and

there is immense clinical value in the early detection and diagnosis of long-term opioid effects. If our societal goal is to achieve the maximal developmental outcomes for all children, then uniform and robust program will be necessary. Although some children might ultimately benefit more than others, however, that can be attributed to a biological variability in response to therapy, other psychosocial factors, or presently unknown factors that require further scientific investigation.

- 2) Children with NAS are at higher risk for a variety of adverse outcomes as noted above. Therefore, they are worthy of a more structured and specialized program of monitoring and surveillance with scheduled extra assessments, for at least two reasons. First, their families/caregivers want to know if their child is healthy and growing and developing normally, and they want to know about the health or other problems likely to be encountered in the future. Special concerns often arise at childhood or social transition points, such as entering childcare or changing school levels, thus requiring careful guidance and advice. Second, most of their developmental problems can be ameliorated or prevented if detected early – identification of high-risk groups for targeted interventions can be both cost-effective and efficient. Multidisciplinary advice from Doyle et al. (2014)¹⁵⁰ was used to design the monitoring protocol as outlined below.
- 3) If these periodic diagnostic medical exams identify a particular deficit or disability, the child's caregivers must be provided access to the specific resources and treatment(s) that they will need to overcome the long-term impacts of NAS. Additionally, caring for a victim of NAS is difficult, associated with increased risks for repeated hospitalizations of the child. An educational program aimed at increasing the understanding of NAS in parents and other caregivers is recommended, including access (or referral) to resources for both the caregiver and the child.
- 4) Barriers for implementing standardized monitoring protocols must be anticipated and addressed. These may include providing funding for transportation to scheduled assessments or making the transport arrangements, providing token compensation to participants, facilitating access by offering home visits or assessments at a location convenient for the parent/caregiver, consideration for living situation, and other barriers.
- 5) Most of these assessments are required annually, unless specified otherwise. Certain specialist assessments may be required only once (e.g., cardiology evaluation to rule-out congenital heart disease), or to be determined by the results of the previous testing – more frequent assessments will be required for the NAS children with abnormal/atypical results.
- 6) The data gained from these assessments must be deidentified, aggregated and securely stored in a state-level database, with query access available to researchers, practitioners, social or healthcare agencies, advocacy groups and others.

In conclusion, implementation of the studies referenced herein as well as the long-term care and treatment of these babies is essential to the resolution of the Opioid Crisis and its impact on our society. This report is based upon the information available at the time it was prepared. With the recent increase in NAS cases, the scientific understanding of NAS and the outcomes of NAS victims continues to evolve. And yet, much work remains to be done, which is the goal of implementing a long-term Court-appointed Science Panel – to study the results of the monitoring and surveillance and to recommend interventions as needs arise. With the Court's permission, I

would like to reserve the right to update this report in order to reflect the accumulating scientific and medical evidence as necessary.

I certify under penalty of perjury that the foregoing is true and correct.

Executed on December 8, 2019.



Dr. Kanwaljeet S. Anand,
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